Mycosis Fungoides

The most common Cutaneous T-cell Lymphoma.

The etiology is unKnown.

① Genetic ② Environmental exposure to Persistant antigenic stimulation

eg ▸ Industerial chemicals, metals, pesticides

▸ Infection: Human T-cell lymphotropic virus / HIV / EBV / CMV / HSV

③ Immunological Factors:-

▸ In early stages (Plaque, Patch) Tcell shows cyto Kine profile of Th1 and secret (IFNγ, IL 2, IL 12)

▸ In late stage (Tumour) Tcell show Th2 and secretion (IL 4, 5, 10)

C/P and histopathology:-

- Rare affect old adults, men > Women, before Diagnosis the pt have Nonspecific Eczematous or psoriasiform skin Lesion.

C/P

patch
- erythematous, scaly, pruritic
- on buttocks, bathing suit
- poikiloderma atrophicans Vasculare (PAV) variants
- patches with mottled hyper/hypopigmentation, Atrophy Telangiectasia.

plaque
- Sharply demarcated, slightly indurated plaque, erythematous or violaceous in color, ↑pruritic
- fusion of adjecent lesions with central resolution may result in geographic appearance (Islands of Normal Skin)

H/P

- Non specific, superfacial band like (Lichenoid) infiltrate of Atypical lymphocyte
- epidermotropism → suggest MF (movement of lymphocyte toward epiderms)
- polymorphous infiltrate (histiocytes, Eosinophils, lymphoid)
- **Mycosis cells** in derms: T-lymphocytes with hyperchromatic, irregular nuclei
- **Epidermotropism**: dyskeratosis
  - Scattered MN cells Surrounded with a halo in epiderms without spongiosis
- Pautrier microabscess: small intra epidermal groups of MN cells located within a vacule

Large mass of pagetosis cells that extend to S.C Fat.
+ epidermotropism, Microabscess
the infiltrate shows many cell with blastic transformation

tumour: Multiple - non pruritic
dome or irregular shape
Flesh color, soft nodule
eroded surface → ulceration
pt in this stage have CMI defect

Extra Cutaneous manifestations :-

- is rare. affect (Lymph nodes 75% — Lungs 60% - Spleen 60% — Liver 60%. it's more common in later phases of MF.
- circulating Sézary cells are found in 18-20% of pt.

Diagnosis

① Immunophenotyping → CD_3, CD_4 +ve / CD_7, CD_8 -ve

② Immunogenotyping (TCRGR) T-cell Receptor gene Rearrangment by Southern blot method or PCR

③ DNA cytophotometry as malignant cells has hypertetraploid DNA → Help in early diagnosis of MF.

④ Lymphocyte Nuclear Contour Index (NCI) by electron microscope examination.

staging of MF

TNM1 staging

T skin

T_0	Lesion suggest MF clinically or H/Pathologically.
T_1	Limited plaques, eczematous (Cover 10% of skin)
T_2	General plaques, erythematous patch (Cover ≥ 10 of skin)
T_3	Cutaneous tumor.
T_4	Generalized erythroderma.

N Lymph nod

N_0	No palpable LN + –ve CTCL pathology
N_1	palpable LN + " "
N_2	No palpable LN + +ve CTCL pathology
N_3	palpable LN + +ve CTCL pathology.

M Viscera (Metastasis)

M_0	No visceral involvement
M_1	Visceral involvement

B Blood

B_0	Atypical circulating cells Not present
B_1	" " are present

Stage	T	N	M
IA	1	0	0
IB	2	0	0
IIA	1–2	1	0
IIB	3	0–1	0
III	4	0–1	0→
IVA	1–4	2–3	0
IVB	1–4	0–3	1

Treatment of MF

① early stage: pre mycotic stage
- Superpotent Topical CST or Intralesional
- UVB if not improved → PUVA
- Topical chemotherapy.
- Retinoids (Bexarotene) – (Acitretin)
- IFN-γ

② Late stage IIB
① Immuno modulators (IFNγ – Retinoids)
② single agent chemotherapy (Methotrexate - etoposide)

③ Stage III
① multimodulatary therapy ② Methotrexate
③ Extra corporeal photopheresis: ECP
the Rx of choice erythrodermic MF, SS

④ Stage IV
1. Multi agent chemotherapy.
2. Palliative Local radiation
3. Bone Marrow/Stem cell transplant.

q3

4. Lymphomatoid Papulosis

- Lymphomatoid papulosis is a **chronic recurrent self-healing** eruption of papules and small nodules with the histological features of CTCL.
- Etiology is unknown.
- 10-20% of cases are preceded, concomitant with or followed by another type of lymphoma, usually MF or Hodgkin lymphoma.

Clinical features:

- **Age:** Mainly young adults.
- **Sites:** Mainly trunk and proximal extremities.
- **Lesions:** An eruption of reddish brown papules or small nodules. They **erupt and rapidly grow over a few days.** Lesions commonly ulcerate with necrotic centers. **Spontaneous resolution** occurs within a few weeks with atrophic scars. The **cycle recurs** every few months.

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Histopathology:

- Three histological subtypes are described:
  1- Type A (Histiocytic)
  2- Type B (Mycosis fungoides-like) هو ده المهم
  3- Type C (Anaplastic large cell lymphoma-like)☆ ☆☆☆☆

Immunophenotype: Large neoplastic cells are:

- **CD30+** ☆☆☆☆☆
- CD3+, CD4+, CD8-

Immunogenotype:

- TCRGR showed that atypical CD30+ large cells have a common clonal origin.

DD

- Pityriais lichenoides (PLEVA, PLC): younger age, short-lived (no recurrence), no nodules, never or rare malignant lymphoma, CD30+ blast cells are NOT seen
- Folliculitis
- Arthropod bite

Treatment:

- As the disease is self-limiting, most patients do not require specific treatment.
- **Systemic therapy:** Systemic steroids – Phototherapy: NB-UVB, PUVA – Methotrexate - Interferon-α2a - Systemic retinoids.

Q4 SC panniculitis T-cell lymphoma

It is defined as a cytotoxic T-cell lymphoma, characterized by the presence of primary subcutaneous infiltrates of small and medium or large sized pleomorphic T-cells α/β^+ in association with many Macrophages.

It is of $CD3+$ $CD4-$ $CD8+$ T-cell phenotypes characterized by subcutaneous nodules which rarely ulcerate and also plaques.

Haemophagocytic Syndrome is uncommon in these cases with survival (5 years) $> 80\%$.

Treatment

Systemic corticosteroids

Subject: Day: Date: / /

Qs-1

(5) Role of Dermatologist in diagnosis of Hodgkin's disease —

(1) Nonspecific lesions: they are very common. occuring in about 30-50% of the cases. they caused mainly by:

(1) pruritus: associated to pigmentation and pruriigo that starts on the legs.

(2) Acquired ichthyosis

(3) Herpes Zosber

(4) Alopecia, exfoliative dermatitis and erythema nodosum

Subject:

Q 5-2

(1) Specific lesions : they are very rare

* Histopathology :

the presence of Reed-Sternberg cells is essential for the histologic diagnosis of Hodgkin disease. there is a polymorphous infiltrate of lymphocytes, polymorphonuclear leucocytes. eosinophils plasma cells. histiocytes and Fibroblasts.

* Treatment : @ nonspecific skin lesions :

symptomatically

(2) specific skin lesions = radiotherapy

DD between cutaneous B-cell lymphoma (CBCL) and pseudolymphomas (PL) (Burg et al., 1994b)

HL

	CBCL (%)	PSL (%)
Clinical		
• No., distribution & localization of skin lesions	• Solitary or multiple & generalized monomorphous (100%)	• Solitary, head (80%)
• Extracutaneous involvement	• Present (100%)	• Absent (100%)
• Type & response to therapy	• Aggressive, TR	• Nonaggressive, CR
• Fatal outcome	• Likely	• No
• Recurrences	• Always	• Rare (< 10%)
• Cure	• Not possible	• Possible
• Survival time	• Affected	• Normal
Histologic		
• Infiltrate covering all levels of the dermis	• Mostly (> 70%)	• Rarely (< 5%)
• Pattern of infiltrate	• Diffuse or nodular, bottom > top heavy	• Nodular (> 90%) top>bottom, heavy
• Follicular center formation (H & E)	• Usually absent	• Usually present
• Transformation into blast form (centroblastic, immunoblastic)	• May occur	• Never occurs
• Eosinophilic granulocytes	• Usually absent	• Always present
Phenotypical		
• Monotypic kappa or lambda light chain reaction of surface immunoglobulin	• Present (100%)	• Absent (100%)
• % of cells expressing B-cell markers (CD20, MB2, CD45R)	• High (> 50%)	• Medium, (50% or less)
• T-cell markers (CD43, CD45RA, CD45RO)	• Low (< 50%)	• Medium, (50% or more)
• Network of CD21 +ve dendritic reticulum cells	• Mostly absent	• Mostly present, regular

TR = temporary response; CR = complete response.

q6

Q 9 - 1

Subject _____ Day _____ Date 1 1

C

Lymphocytic infiltration of jessner

It is characterized by a symptomatic well demarcated, slightly infiltrated, smooth erythematous nodules and plaques sometimes with central clearing usually located on face. It heals without scarring but recurrence may occur

×Histopathology: Normal or flat epidermis. perivascular perifollicular patchy lymphocytic infiltrate in epidermis & cells

Q7-2

Subject: Day: Date: / /

* pathogenesis: it is initial phase of DLE or pLE

* treatment:

(1) topical or intralesional steroids.

(2) Antimalarials.

* Lymphocytoma cutis:

It affects women more commonly the face especially the ear comm affected, It is a solitary papule, nodu or plaque. Form, skin colored, red or violaceous.

Q7-3

Subject: Day: Date: / /

Histopathology: heavy dermal infiltrate, separated from epidermis by a narrow Grenz zone of normal collagen, the infiltrate consists of 2 types of cells, small and large Lymphocytes, at the periphery of the infiltrate single rows of lymphocytes. Found in a Flem this condition are B-cells.

*treatment: ① topical or intra lesional steroids.

② Radiotherapy ③ penicillin

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lymphoma

Q8-1

H/P of MF ?

(1) premycotic stage : Non specific or Epidermotropism -

- Epidermotropism → presence of Mononuclear cells surrounded by ahalo within the epidermis without spongiosis.

(2) plague stage.

a) polymorphous cellular infiltrate {histiocytes eosinophils, plasma cells, lymphoid cells} in abaand like pattern in upper dermis.

b) Mycosis cells : in dermal infiltrate. They are T. lymphocytes & hyperchromatic & irregular Nuclei

c) Epidermotropism : Diagnostic : Mononuclear cells surrounded by halo within the epidermis without spongiosis.

Q8-2 lymphoma

- Pautrier Microabsesses : Consists of small intra epidermal groups of Mononuclear cells located within ovacule.

(3) Tumor stage :

Masses of Mycosis cells extend into subcutaneous fat

- Epidermotropism of pautrier Microabsesses rarely seen.
- plastic transformation of some cells may be present.